

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
8 July 2004 (08.07.2004)

PCT

(10) International Publication Number
WO 2004/056832 A3

(51) International Patent Classification⁷: C07D 493/04,
417/06, A61K 31/427, A61P 35/00, C07C 59/90 // (C07D
493/04, 313:00, 303:00)

CH-4456 Tenniken (CH). SEDELMEIER, Gottfried
[DE/DE]; Erlenweg 11, 79227 Schallstadt (DE).

(21) International Application Number:
PCT/EP2003/014747

(74) Agent: GRUBB, Philip; Novartis AG, Corporate Intellectual
Property, CH-4002 Basel (CH).

(22) International Filing Date:
22 December 2003 (22.12.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR,
CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY,
TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0230024.2 23 December 2002 (23.12.2002) GB

(84) Designated States (*regional*): Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR).

(71) Applicant (*for all designated States except AT, US*): NO-
VARTIS AG [CH/CH]; Lichtstrasse 35, CH-4056 Basel
(CH).

Published:
— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

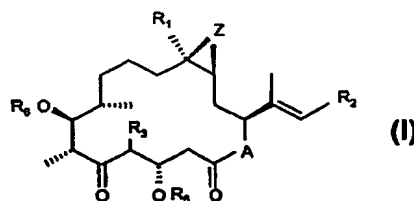
(71) Applicant (*for AT only*): NOVARTIS PHARMA GMBH
[AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventors; and
(75) Inventors/Applicants (*for US only*): DENNI-DIS-
CHERT, Donatienne [FR/FR]; 39 rue des Clefs, F-68000
Colmar (FR). FLOERSHEIMER, Andreas [DE/CH];
Lehmenweg 38, CH-4143 Dornach (CH). KÜSTERS,
Ernst [DE/DE]; Gallenweilerweg 1, 79427 Eschbach
(DE). OBERER, Lukas [CH/CH]; Schlossgasse 17,

(88) Date of publication of the international search report:
10 September 2004

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: EPOTHILONE DERIVATIVES



(57) Abstract: The present invention relates to C4-demethyl-epothilones or C4-bisnor-epothilones of Formula (I), their pharmaceu-
tical use, pharmaceutical composition containing the same and methods for their preparation.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/14747

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D493/04 C07D417/06 A61K31/427 A61P35/00 C07C59/90
//(C07D493/04, 313:00, 303:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, BEILSTEIN Data, CHEM ABS Data, BIOSIS, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, Y	WO 99/65913 A (BIOTECHNOLOG FORSCHUNG GMBH ; GERTH KLAUS (DE); SASSE FLORENZ (DE);) 23 December 1999 (1999-12-23) see compounds 5,6,16-19	1-13
X, Y	HARDT I H ET AL: "New Natural Epothilones from Sorangium cellulosum, Strains So ce90/B2 and So ce90/D13: Isolation, Structure Elucidation, and SAR Studies" JOURNAL OF NATURAL PRODUCTS, XX, XX, vol. 64, no. 7, July 2001 (2001-07), pages 847-856, XP002220541 ISSN: 0163-3864 See compounds 5,6,16-19	1-13



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

29 April 2004

Date of mailing of the international search report

15. 07. 2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Steendijk, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/14747

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98/25929 A (CIBA GEIGY AG ; SARABIA FRANCISCO (ES); VALLBERG HANS (SE); NICOLAO) 18 June 1998 (1998-06-18) pages 2-3; figure 13	1-13
Y	NICOLAOU K C ET AL: "Chemical Biology of Epothilones" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, VERLAG CHEMIE. WEINHEIM, DE, vol. 37, no. 15, August 1998 (1998-08), pages 2014-2045, XP002131418 ISSN: 0570-0833 page 2026	1-13
A	PATENT ABSTRACTS OF JAPAN vol. 015, no. 193 (C-0832), 17 May 1991 (1991-05-17) & JP 03 048641 A (MITSUBISHI KASEI CORP), 1 March 1991 (1991-03-01) abstract	1-13
A	SU D S ET AL: "Structure-activity relationships of the epothilones and the first in vivo comparison with paclitaxel" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, VERLAG CHEMIE. WEINHEIM, DE, vol. 36, no. 19, 17 October 1997 (1997-10-17), pages 2093-2096, XP002137123 ISSN: 0570-0833 cited in the application page 2094, left-hand column	1-13
P,X	WO 03/022844 A (SLOAN KETTERING INST CANCER ; LEE CHULBOM (US); RIVKIN ALEXEY (US);) 20 March 2003 (2003-03-20) page 45	1-10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/14747

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-13

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-13

C4-demethyl-epothilone derivatives, their preparation and intermediates (III and IV) specific for the preparation of C4-demethyl-epothilone derivatives

2. claim: 14

Preparation of intermediate of formula II

3. claims: 15,16

Isolation of C4-desmethyl-epothilone B involving chromatography on Chiralpak-AD column

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/14747

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9965913	A	23-12-1999	DE 19826988 A1	23-12-1999
			AT 248174 T	15-09-2003
			AU 757452 B2	20-02-2003
			AU 4899599 A	05-01-2000
			CA 2336189 A1	23-12-1999
			DE 59906782 D1	02-10-2003
			DK 1087975 T3	01-12-2003
			WO 9965913 A2	23-12-1999
			EP 1275648 A1	15-01-2003
			EP 1087975 A2	04-04-2001
			ES 2207249 T3	16-05-2004
			JP 2002518397 T	25-06-2002
			PT 1087975 T	30-01-2004
			SI 1087975 T1	31-12-2003
			US 2004049051 A1	11-03-2004
			US 6624310 B1	23-09-2003
WO 9825929	A	18-06-1998	US 6441186 B1	27-08-2002
			AU 746597 B2	02-05-2002
			AU 5757798 A	03-07-1998
			BR 9714140 A	29-02-2000
			CA 2274833 A1	18-06-1998
			CN 1246862 A ,B	08-03-2000
			WO 9825929 A1	18-06-1998
			EP 0944634 A1	29-09-1999
			JP 2001504856 T	10-04-2001
			US 6380394 B1	30-04-2002
			US 6660758 B1	09-12-2003
JP 03048641	A	01-03-1991	NONE	
WO 03022844	A	20-03-2003	WO 03022844 A2	20-03-2003
			US 2003176368 A1	18-09-2003